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| 09/936,565 | 02/04/2002 | John J. Sauk | UNIMD 4 | 7145 |

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| EXAMINER | |
|---|---|
| YAEN, CHRISTOPHER H | |
| ART UNIT | PAPER NUMBER |
| 1643 | |

DATE MAILED: 02/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/936,565 | SAUK, JOHN J. | |
| | Examiner | Art Unit | |
| | Christopher H. Yaen | 1643 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *19 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) *1-23,27 and 28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-26 and 29-32* is/are rejected.

7)☒ Claim(s) *24 and 25* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/9/02, 10/16/02,* 6/26/03
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

***Re: Sauk JJ***

### *Election/Restrictions*

1. Applicant's election with traverse of group XXXI (claims 24-26 and 29-32 SEQ ID No: 1) in the reply filed on 10/19/2004 is acknowledged. The traversal is on the ground(s) that all claims of the instant invention comprise overlapping subject matter and it would not be an undue burden to search all the claims together. This is not found persuasive because arguments of "undue burden do not apply when restriction is required under 35 USC 121 and 372, as in the instantly filed application. Thus, when the Office considers international applications as an International Searching Authority, as an International Preliminary Examining Authority, and during the national stage as a Designated or Elected Office under 35 U.S.C. 371, only PCT Rule 13.1 and 13.2 will be followed when considering unity of invention of claims of different categories without regard to the practice in national applications filed under 35 U.S.C. 111. Thus, it is maintained that the technical feature linking the inventions of Groups I-LIV does not constitute a special technical feature as defined by PCT Rule 13.2 and does not define a contribution over the prior art for the reasons of record.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 1-32 are pending, claims 1-23 and 27-28 are withdrawn from further consideration as being drawn to non-elected subject matter.

3. Claims 24-26 and 29-32 are examined on the merits.

***Information Disclosure Statement***

4. The Information Disclosure Statements filed 5/9/02, 10/16/02, and 6/26/03are acknowledged and considered. Signed copies of the IDSs are attached hereto.

***Claim Objections***

5. Claims 24-25 are objected to because of the following informalities:

a. Claims 24-25 are objected to because the claims recite subject matter that is drawn to non-elected subject matter. Specifically, the claims recite SEQ ID No: 2.

Appropriate correction is required.

***Claim Rejections - 35 USC § 101***

6. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 24-25 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claims 24-25, as written, do not sufficiently distinguish over peptides/polypeptides as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. *See Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended

to indicate the hand of the inventor, e.g., by insertion of "Isolated" or "Purified" as taught on page 10 of the specification. See MPEP 2105.

### *Claim Rejections - 35 USC § 112, 1st paragraph*

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 29 and 31-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The written description in this case has only set forth an isolated peptide of SEQ ID No: 1 or a pharmaceutical composition comprising a peptide of SEQ ID No: 1, and therefore the written description is not commensurate in scope to the claims that read on any "agent" or a pharmaceutical composition comprising any "agent" as claimed. The following *written description* rejection is set forth herein.

The claims recite an "agent" as part of the invention. However, there does not appear to be an adequate written description in the specification as-filed of the essential structural features that provides the function of targeting or binding to surface localized Hsp47, as claimed. The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient

description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 3rd column).

Applicant does not appear to have reduced to practice the broad genus of agents as claimed. Such agents include antibodies, peptides, nucleotide sequences, organic and inorganic compounds, etc. Neither has Applicant provided a sufficient written description of any structure that may be correlated with the desired targeting or localization function. Moreover, to provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The specification provides description for antibodies and peptides, however, no other structural information has been provided for the vast array of agents that are encompassed by the term. An "agent" encompasses *any* molecule with the functional activity of targeting or localizing to the surface expressed Hsp47. However, this functional activity (i.e. binding to Hsp47) is not sufficient to identify the encompassed molecules. There is no common structure or distinguishing characteristic required for such a wide variety of activities. Thus the genus of compounds encompassed by this term is extensive and the artisan would not be able to recognize that Applicant was in possession of the invention as now claimed.

Consequently, Applicant was not in possession of the instant claimed invention. See Regents of the University of California v. Eli Lilly and Co. 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). Adequate written description of genetic material "'requires a precise definition, such as by structure, formula, chemical name, or physical properties,' not a mere wish or plan for obtaining the claimed chemical invention." Id. 43 USPQ2d at 1404 (quoting Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606). The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter of the claim. Id. 43 USPQ2d at 1406. A description of what the genetic material does, rather than of what it is, does not suffice. Id.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001. Applicant is invited to point to clear support or specific examples of the claimed invention in the specification as-filed.

***Claim Rejections - 35 USC § 112, 1st paragraph***

9. Claims 29, 31, and 32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a peptide of SEQ ID No: 1 which binds to a surface expressed Hsp47 or a pharmaceutical composition comprising said peptide, does not reasonably provide enablement for any agent the binds to a surface expressed Hsp47 or a pharmaceutical composition comprising said agent. The specification does not enable any person skilled in the art to which it pertains, or with

which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). Wands states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

***The nature of the invention***

The claims are drawn generically to an agent or a pharmaceutical composition comprising said agent that binds to a surface expressed Hsp47 molecule. The invention is in a class of invention which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." *Mycogen Plant Sci., Inc. v. Monsanto Co.*, 243 F.3d 1316, 1330 (Fed. Cir. 2001).

***The breadth of the claims***

The claims encompass molecules such as organic or inorganic molecules, nucleotide sequences, and peptide mimetics, for example. Because the claims are broadly drawn to any agent, the claims read on nucleotide sequences or the use of nucleotide sequences for the purposes of gene therapy.

***The unpredictability of the art and the state of the prior art***

At the time the application was filed, the art of administering any type of genetic expression vector to an individual so as to provide a tangible therapeutic benefit was poorly developed and unpredictable. The NIH ad hoc committee to assess the current status and promise of gene therapy reported in December 1995 that "clinical efficacy has not been definitively demonstrated at this time in any gene therapy protocol, despite anecdotal claims...," and that "significant problems remain in all basic aspects of gene therapy" (Orkin and Motulsky, p. 1). In a review article published in Scientific American in June 1997, Theodore Friedmann discusses the technical barriers which have so far prevented successful gene therapy, and states "So far, however, no approach has definitively improved the health of a single one of the more than 2,000 patients who have enrolled in gene therapy trials worldwide" (p. 96). In a review article published in Nature in September 1997, Inder Verma states "Although more than 200 clinical trials are currently underway worldwide, with hundreds of patients enrolled, there is still no single outcome that we can point to as a success story" (p. 239).

In an article published well after the effective filing date of the instant application, Rubanyi (2001) teaches that the problems described above remain unsolved at the time the instant application was filed. Rubanyi states, "[a]lthough the theoretical advantages of [human gene therapy] are undisputable, so far [human gene therapy] has not delivered the promised results: convincing clinical efficacy could not be demonstrated yet in most of the trials conducted so far ..." (page 113, paragraph 1). Among the technical hurdles that Rubanyi teaches remain to be overcome are problems with gene delivery vectors and improvement in gene expression control systems (see especially the section under "3. Technical hurdles to be overcome in the future", pp. 116-125).

The state of the art is such that no correlation exists between successful expression of a gene and a therapeutic result (Ross et al., p. 1789, column 1, paragraph 1).

***Working examples***

The working examples provided in the specification discuss the use of antibodies to the surface expressed Hsp47 or peptides (discovered through phage display screening methods) that target the surface expressed Hsp47.

***Guidance in the specification***

The specification provides little to no guidance in terms of any other agent that may be used for the purposes of targeting the surface expressed Hsp47 as claimed. Moreover, the specification provides no nexus between the function of the antibodies or peptides that bind to the surface expressed Hsp47 and any other agent encompassed by the term.

***Level of skill in the art***

The level of skill in the art is deemed to be high.

***Conclusion***

Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that ad, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, the presence of a working example which does not address the issue of the efficacy of the control and the negative teachings in the prior art balanced only against the high skill level in the

art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claim as broadly written.

***Claim Rejections - 35 USC § 102***

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 24-26, and 29-31are rejected under 35 U.S.C. 102(b) as being anticipated by Noteborn *et al* (WO 95/03414). The claims of the instant invention recite the term "comprising", which is considered open-ended claim language and includes amino acid residues outside of the specified polypeptide antigen specificity. Therefore, a peptide "comprising" SEQ ID No: 1 includes an unlimited number of amino acid sequences flacking either side of the claimed sequence.

Noteborn *et al* teach a VP3 protein of a chicken anemia virus comprising the sequence of SEQ ID No: 1 (see figure 3 amino acids 14-25). Thus, the protein is not a full length collagen, not naturally occurring collagen, nor a fragment thereof. In addition, Noteborn *et al* also teach that the protein can be used as a vaccine for the treatment of tumors (see page 1 and 5, for example) and thus would inherently comprise a pharmaceutical carrier. Moreover, because the term "agent" encompasses peptides or

polypeptides, the claims reciting the term "agent" are also anticipated by Noteborn for the same reason as applied to the peptide.

Although the polypeptide taught by Noteborn *et al* is not specifically characterized as having the functional limitation of binding to and modulating a cell expressing surface Hsp47 or generating a cytostatic or cytolytic effect as claimed, the claims are drawn to the product *per se*, and in the absence of evidence to the contrary, the polypeptide as taught by Noteborn *et al* would have the said functions. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the polypeptide of the prior art is any different from the claimed sequence of SEQ ID No: 1. In the absence of evidence to the contrary, the burden is on the applicant to prove that the sequence claimed is different from that taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

***Claim Rejections - 35 USC § 102***

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

13. Claims 24-26 and 29 are rejected under 35 U.S.C. 102(b) as being anticiapted by Homma MK *et al* (Cell Growth and Differentiation 1996 March;7(3):281-288). Homma

MK *et al* teach a peptide that falls within the motif requirements of SEQ ID No: 1 (see page 282 figure 1B, for example), that is a PCI peptide. Thus, the protein is not a full length collagen, not naturally occurring collagen, or a fragment thereof. Because the term "agent" encompasses peptides or polypeptides, the claims reciting the term "agent" are also anticipated by Homma Mk *et al* for the same reason as applied to the peptide.

Although the polypeptide taught by Homma *et al* is not specifically characterized as having the functional limitation of binding to and modulating a cell expressing surface Hsp47 or generating a cytostatic or cytolytic effect as claimed, the claims are drawn to the product *per se*, and in the absence of evidence to the contrary, the polypeptide as taught by Homma MK *et al* would have the said functions. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the polypeptide of the prior art is any different from the claimed sequence of SEQ ID No: 1. In the absence of evidence to the contrary, the burden is on the applicant to prove that the sequence claimed is different from that taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

***Claim Rejections - 35 USC § 102***

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the

> applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

15. Claims 24-26 and 29-32 are rejected under 35 U.S.C. 102(e) as being anticipated by Nestor *et al* (US Patent 5,783,179). Nestor *et al* teach a peptide of SEQ ID No: 1 (see col. 13 and 14), which falls within the criteria established by SEQ ID No: 1 as claimed in the instant invention. Moreover, the sequence as taught by Nestor *et al* is derived from amino acids residues 174-185 of C-reactive protein and therefore not a full length collagen, not naturally occurring collagen, nor a fragment thereof (see abstract for example). Because the term "agent" encompasses peptides or polypeptides, the claims reciting the term "agent" are also anticipated by Nestor *et al* for the same reason as applied to the peptide. In addition, Nestor *et al* also teach that the peptides can be used as pharmaceutical compositions, wherein the peptide of SEQ ID No: 1 further comprises a pharmaceutical carrier (see col. 5, lines 20-67).

Although the polypeptide taught by Nestor *et al* is not specifically characterized as having the functional limitation of binding to and modulating a cell expressing surface Hsp47 or generating a cytostatic or cytolytic effect as claimed, the claims are drawn to the product *per se*, and in the absence of evidence to the contrary, the polypeptide as taught by Nestor *et al* would have the said functions. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the polypeptide of the prior art is any different from the claimed sequence of SEQ ID No: 1. In the absence of evidence to the contrary, the burden is on the applicant to prove that the sequence claimed is different from that taught by the prior art and to establish

patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

***Conclusion***

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H. Yaen whose telephone number is 571-272-0838. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, Ph.D. can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Christopher Yaen, Examiner
Art Unit 1643
February 16, 2006

CHRISTOPHER YAEN
PATENT EXAMINER